UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,218	07/24/2006	Marie-Noelle Bizot	4-32908A	4236

67283 7590 08/25/2009

MONTGOMERY, MCCRACKEN, WALKER & RHOADS, LLP
123 SOUTH BROAD STREET
AVENUE OF THE ARTS
PHILADELPHIA, PA 19109

EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,218	BIZOT ET AL.	
	Examiner	Art Unit	
	NABILA G. EBRAHIM	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9,13,16 and 17* is/are pending in the application.

4a) Of the above claim(s) *16-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,13,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt of Claims' amendments and Applicant's remarks dated 5/26/2009 is acknowledged.

Claim Rejections - 35 USC § 112

In view of the amending the claims the rejection of claims 1, 5, 7-9, 13, and 15 are rejected under 35 U.S.C. 112, second paragraph is hereby withdrawn.

Election/Restrictions

Newly submitted claims 16 and 17 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims recites a method of administering a partitionalble dose of tegaserod comprising administering by oral ingestion an amount of a homogenous suspension. The product as claimed can be used in a materially different process of using that product other than administering a partitionable dose such as administering the product in a masked or improved taste. See MPEP § 806.05(h).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 16-17 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1, 8, 9, and 13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over DE BRUIJN et al. WO0010526 (De Bruijn) in view of Patel et al. US 20030180352 (Patel) and further in view of the combination of [Achong et al. US 20040162273 (Achong), Belcheff US 20010031283 (Belcheff), Naicker et al US 7060672 (Naicker) and Allen et al. Stability of ramipril in water, apple juice, and applesauce. Am J Health Syst Pharm. 1995 Nov 1;52(21):2433-6, abstract (Allen)].

De Bruijn teaches a pharmaceutical composition, in particular to a composition for administering active agents which are poorly soluble in aqueous media, and/or which are acid sensitive (abstract). The composition comprises tegaserod (pages 5, and 7) or its salt (page 5) and is prepared to have dissolution in water of about 30%-90% in 5 minutes (page 7). The composition could be in the form of tablets among other preparations (page 13). The compositions of the invention were packed in conventional manner to keep out humidity, e.g., in a blister pack, optionally with a desiccant (page 17). Regarding claims 8 and 9 that recite amount of tegaserod in the dosage form of 6 mg or 2 mg. De Bruijn teaches that a tablet may have different amounts according to the condition it is used, for example for irritable bowel syndrome (IBS), 1 mg to 12 mg of active agent is used in the tablet (page 9).

Claims 5-9 recite "a crushed tablet" which reads on a chewable tablet, powder, granulate, bead etc. comprising the tegaserod. From these preparation De Bruijin discloses granulates and compressed tablets (page 19).

New amendments to claim 1 reciting "pharmaceutically acceptable salt thereof suspended therein" would not distinguish instant claims over the prior art because

DeBruijn's teaches that tegaserod could be prepared in the form of a suspension (page 13).

De Bruijn does not teach literally a crushed tablet or beverage.

Patel teaches solid carriers for improved delivery of active ingredients in pharmaceutical compositions. The composition is meant to mask the taste of unpalatable pharmaceutical active ingredients [0028]. Patel suggests agents of the unpalatable drugs among which is tegaserod [0058] and the dosage form can be a powder or a multiparticulate, such as a granule, a pellet, a bead, a spherule, a beadlet, a microcapsule, a millisphere, a nanocapsule, a nanosphere, a micro sphere, a platelet, a minitablet, a tablet or a capsule [0229]. The composition of the invention can be administered as a chewable tablet, a quick or fast dissolving tablet, an effervescent tablet, a buccal or sublingual solid, a granule, a film, a sprinkle, a pellet, a bead, a pill, a powder, a triturate, a platelet, a strip or a sachet. Compositions can also be administered as" dry syrup", where the finished dosage form is placed directly on the tongue and swallowed or followed with a drink or beverage ([0272], see also claims 24 and 47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Patel to De Bruijn because Patel teaches a way for masking the unpleasant taste for the tegaserod.

Neither of the references disclosed apple juice as a beverage with the tegaserod.

The combination of Achong, Belcheff, Naicker and Allen are relied upon as follows:

Achong teaches powder pharmaceutical composition. The reference discloses that powder pharmaceutical compositions can also be formulated to contain aesthetically pleasing flavor and sweetener ingredients [0008]. When the powder pharmaceutical compositions can be dissolved in a liquid, such as cold water, ice tea, orange juice, grape juice, and apple juice [0028].

Belcheff teaches a natural extract comprising: providing a quantity of pursiane provided in apple juice which is used as preservative (see claims 1 and 6).

Naicker teaches a pharmaceutical composition comprising cyclosporine analogue dissolved in an aqueous media such as a fruit juice specifically apple juice (see claims 1 and 19) wherein the formulations form stable microemulsion preconcentrates and may provide superior drug bioavailability and/or may reduce one or more adverse effects associated with the administration of cyclosporine (abstract)

Allen researched the stability of ramipril in water, apple juice and applesauce and found that ramipril from 1.25-, 2.5-, and 5-mg capsules mixed in water, and in apple juice was stable for 24 hours at 23 degrees C and for 48 hours at 3 degrees C.

In view of the above explained disclosures, it is clear that the art knew the benefits of apple juice as a preservative, a taste masking agent, a bioavailability providing agent, an agent to reduce adverse effects, and a stabilizing agent. Note that the active agents disclosed in the prior arts relied upon are totally different in structure and effect which would motivate a person of ordinary skill in the art to choose from a finite number of predictable option of using apple juice to facilitate swallowing a tablet of tegaserod with a reasonable expectation of success of producing a tegaserod in apple

juice formulation. I would also be obvious to a person of ordinary skill to partition the dose of tegaserod because Allen showed that a drug can be stabilized in apple juice for 24 hours and Belcheff teaches that apple juice has a preservative effect.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the tablet disclosed by De Bruijn or Patel's tablet, powder, granulate or crushed tablets to apple juice as disclosed by any of Achong, Belcheff, Naicker and/or allen because these references disclose that apple juice has an aesthetically pleasing flavor, a preservative property, a taste masking effect, a bioavailability providing property, properties for reducing adverse effects, and a stabilizing agent. The expected result would be a composition comprising tegaserod or a pharmaceutically acceptable salt swallowed by the use of a beverage or added to a beverage such as apple juice.

Response to Arguments

Applicant's arguments filed 5/26/2009 have been fully considered but they are not persuasive. Applicant argues that:

- Neither DeBruijn nor Patel teach, suggest, or provide motivation to a homogenous oral suspension comprising apple juice and tegaserod to provide administration of a partitioned dose of tegaserod. Neither DeBruijn nor Patel teach the use of crushed tablets of tegaserod containing a known and fixed amount of active ingredient as a component of a homogenous suspension, wherein the dosage of the active ingredient is capable of being partitioned, as expressly recited by Applicant's claims. Patel is directed at solid form compositions such as chewable tablets, film, etc.

Applicant's homogenous oral suspension is an alternative method of tegaserod administration which is especially suitable for partitioning a dosage of tegaserod and for a patient's use at home.

To respond: It is respectfully noted that most of drug formulations are used by patients at home. Being at home while partitioning a tablet and swallowing it or dissolving it in a drink is not inventive or novel. Applicant is arguing an alternative method of administration of tegaserod which is especially suitable for a patient's use at home. However, new claims reciting" a method of administering ..." were withdrawn from consideration since applicant received an office action on the merits for the originally presented invention. The claims are directed towards an oral suspension comprising a beverage consisting of apple juice and a mixture consisting of an effective amount of tegaserod or acceptable salt in the form of at least one of a powder, a .granulate, a .grind, and a pulver of particles. DeBruijn's teaches that tegaserod could be prepared in the form of a suspension (page 13), and that the composition is granulated and sieved (see example 1), Patel teaches a crushed tablet of a drug such as tegaserod is suspended in a beverage. Achong and the combination of (Belcheff, Naicker, and Allen) teach that powder pharmaceutical compositions can be dissolved in a liquid such as apple juice for many advantages such as preservation, stabilization, bioavailability, reducing side effects and taste masking.

- At the time of the invention, tegaserod was not available as an oral solution, or in dosages other than 6 or 2 mg tablets. Moreover, tablets of tegaserod do not have a

partition line. As a result, there was no procedure or method for administering tegaserod in a particular dosage other than 2 mg or 6 mg.

To respond: adjusting a dose by a physician or a pharmacist is within the skills of those highly qualified artisans. In addition, it is not difficult to use two tablets of 2 mg to reach the missing amount of 4 mg. Further, most of drug dosages are filled with specific doses of the drug and still can be adjusted by people skilled in the art. Finally crushing a tablet and adding it to a liquid is used for years for different reasons and not a new approach that is not known in the art or to even to the public.

- Applicant respectfully asserts that Achong, Belcheff, Naicker and Allen fail to cure the defects of the DeBruijn and Patel combination. Applicant asserts that Naicker is not a valid reference for prior art purposes because the patent date of June 13, 2006 is two years after the priority date of Applicant's present Application, which is March 30, 2004. As such, Applicant respectfully requests that the Examiner disqualify Naicker as a reference in the present Action.

To respond: Achong Belcheff, Naicker, and Allen show that apple juice has many advantages that makes it preferred over other liquids in dissolving or suspending different active agents. Apple juice has an aesthetically pleasing flavor, is a preservative property, a taste masking effect, a bioavailability providing property, properties for reducing adverse effects, and a stabilizing agent. Finally, **Naicker is a valid reference** because, the publication date of the Naicker's application (US publication 20030171264) was 9/11/2003 which antedates the instant application priority date of 3/30/2004.

- Applicant has discovered that apple juice has an unexpected advantage and superior results, specifically a superior dissolution profile, when compared to other masking agents discussed in the prior art, (See also Carrier et al. "Stability and Compatibility of Tegaserod from Crushed Tablets Mixed in Beverages and Food' American Society of Health-System Pharmacists, Inc. (2004), Pages 1138 (3d column), 1140 (3d column), and 1141 (middle column), attached hereto as Exhibit A).

To respond: the dissolution rate is not within the scope of instant claims to be compared to the prior art. Further, dissolution is not an unexpected result of the instant claims since independent claim 1 recites a suspension not a solution. Finally, as shown hereinabove in the office action, apple juice has many advantages that make the liquid distinguished over other fruit juices. If Applicant is arguing that apple juice has one more advantage than what is known in the art, then it was decided in court that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established, Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

- Applicant has discovered that the dissolution of crushed tablets of tegaserod in apple juice was complete in five minutes and that the tegaserod was stable in apple juice for up to one hour at room temperature and up to three days when stored properly,

providing a superior dissolution profile when compared to orange juice. (See Example 3 of Applicant's specification; See Carrier, Page 1140).

To respond: Applicant showed in the comparative tests that tegaserod dissolves in water and apple juice in the same profile. Thus, it is not clear if the apple juice has the ability to dissolve it or the water contained in the juice was the reason of the better dissolution. Note that Applicant claims recite a suspension and not a solution. In addition, the stability of the drug is not an unexpected result since Allen researched the stability of ramipril in water, apple juice and applesauce and found that ramipril from 1.25-, 2.5-, and 5-mg capsules mixed in water, and in apple juice was stable for 24 hours at 23 degrees C and for 48 hours at 3 degrees C. Therefore the stabilizing property of apple juice was known in the art before the time of the invention.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NABILA G. EBRAHIM whose telephone number is (571)272-8151. The examiner can normally be reached on 9:00AM - 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nabila G Ebrahim/
Examiner, Art Unit 1618

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618